

## **REMARKS**

Applicants acknowledge the Examiner's withdrawal of all rejections made in the Office Action dated March 25, 2004.

Claims 95, 106, 108, 109, 115-119, 121, 125, 128, 130, 131, and 145-162 are pending in the application.

The amendments to the claims find support in the specification as filed. The amendments to Claim 95 find support in the specification, for example, at page 3, lines 7-12 (paragraph 8) and at page 4, lines 10-23 (see, e.g., lines 20-23) (paragraph 11); and elsewhere in the specification and claims as originally filed. The amendment to Claim 118 defines a term in the claim, as defined in the Sequence Listing as filed. The amendments to Claim 147 delete the term "non-oligomerizing" and find support in the specification, for example, at page 4, lines 10-23 (see, e.g., lines 20-23) (paragraph 11); and elsewhere in the specification and claims as originally filed. The amendment to Claim 148 corrects a grammatical error by adding a period at the end of the claim. The amendments to Claims 154, 156, 157, 158, and 160 delete the term "non-oligomerizing," consistent with Claims 95 and 147.

No new matter is added by way of the claim amendments.

Claims 95, 106, 109, 115-119, 121-125, 128, 130, 131, and 145-162 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabling a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. On slightly different alleged grounds, Claims 95, 106, 109, 115-119, 121, 125, 128, 130, 131, and 145-162 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabling a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

Claims 95, 106, 108, 109, 119, 130, 131, 145, and 146 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. On other alleged grounds, Claims 115-118, 121, 125, 128, and 148-162 stand rejected

under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants respectfully traverse these rejections to the claims.

**The Rejections of Claims 95, 106, 109, 115-119, 121, 125, 128, 130, 131, and 145-162 under 35 U.S.C. §112, First Paragraph**

Claims 95, 106, 109, 115-119, 121, 125, 128, 130, 131, and 145-162 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabling a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. The Examiner acknowledges that the specification provides enablement for a polynucleotide encoding a fluorescent protein with a reduced tendency to oligomerize, wherein the protein is GFP or a fluorescent protein related to GFP and the amino acid sequence has the mutation A206K, L221K, and or F223R. However, the Examiner feels that the specification "does not reasonably provide enablement for a polynucleotide encoding any fluorescent protein having a reduced tendency to oligomerize."

Applicants have amended Claims 95 and 147 for clarity. As amended, Claim 95 is directed to a polynucleotide encoding a chimeric phosphorylation indicator comprising a fluorescent molecule having a reduced tendency to oligomerize and comprising a mutation that corresponds to an A206K mutation, an L221K mutation, an F223R mutation, or an L221K and F223R mutation of SEQ ID NO: 6 or SEQ ID NO: 10. As amended, Claim 147 is directed to a polynucleotide encoding a chimeric phosphorylation indicator having a reduced tendency to oligomerize, and comprising a mutation which corresponds to an A206K mutation, an L221K mutation, an F223R mutation, or an L221K and F223R mutation of SEQ ID NO: 6 or SEQ ID NO: 10.

Applicants submit that Claims 95, 147, and their dependent claims are directed to subject matter that is described in the specification so as to enable one of ordinary skill in the art to practice the invention without undue experimentation. For example, applicants note that the specification (see, e.g., pages 47-60 and elsewhere in the

specification) provides instruction in how to make and use the novel polynucleotides encoding the chimeric phosphorylation indicators, and provides a reasonable number of representative examples of such polynucleotides and their use. In addition, Applicants note that Claims 95 and 147 have been amended to recite subject matter (previously recited in dependent claims) that was acknowledged by the Examiner to be enabled. Accordingly, Applicants respectfully submit that the rejections of Claims 95, 106, 109, 115-119, 121, 125, 128, 130, 131, and 145-162 under 35 U.S.C. §112, first paragraph, are overcome.

**The Rejections of Claims 95, 106, 109, 115-119, 121, 125, 128, 130, 131, and 145-162 under 35 U.S.C. §112, First Paragraph**

Claims 95, 106, 109, 115-119, 121, 125, 128, 130, 131, and 145-162 stand rejected under 35 U.S.C. §112, first paragraph, the Examiner alleging that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

However, as noted above, the specification provides a number of representative examples of the claimed polynucleotides and their use. Applicants provide definitive structural and functional features of the claimed genus, and the claims explicitly recite critical elements of the invention. For example, the Examples at pages 47-60 and Figures 5-7, in addition to the discussion at pages 39-46 and elsewhere in the specification, illustrate and describe the genus and provide specific examples of the claimed polynucleotides. Accordingly Applicants submit that the specification demonstrates that the inventors had possession of the claimed invention at the time the application was filed.

Accordingly, Applicants respectfully submit that the rejections of Claims 95, 106, 109, 115-119, 121, 125, 128, 130, 131, and 145-162 under 35 U.S.C. §112, first paragraph, are overcome.

**The Rejections of Claims 95, 106, 108, 109, 119, 130, 131, 145, and 146 under 35 U.S.C. §112, Second Paragraph**

Claims 95, 106, 108, 109, 119, 130, 131, 145, and 146 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner characterizes Claim 95 as being drawn to a polynucleotide encoding a chimeric indicator having portions, and suggests that Claim 95 is not clear in stating "what the portions are meant to encompass."

Claim 95 was amended to further clarify the claims, and now includes the phrase "having portions comprising a phosphorylatable domain and a fluorescent molecule" as suggested by the Examiner. Applicants believe the claim clearly states what the portions are meant to encompass. Accordingly, Applicants respectfully submit that the rejections of Claims 95, 106, 108, 109, 119, 130, 131, 145, and 146 under 35 U.S.C. §112, second paragraph, are overcome.

**The Rejection of Claims 115-118, 121, 125, 128, and 148-162 Under 35 U.S.C. §112, Second Paragraph**

Claims 115-118, 121, 125, 128, and 148-162 stand rejected under 35 U.S.C. §112, second paragraph, the Examiner characterizing the claims as drawn to "a polynucleotide encoding a fluorescent protein which is non-oligomerizing and it has a reduced tendency to oligomerize" and stating that "A protein cannot be non-oligomerizing while at the same time still form oligomers."

Claims 95, 147, 154, 156, 157, 158, and 160 have been amended for clarity to delete the term "non-oligomerizing." Applicants believe the claims clearly indicate that the fluorescent proteins have a reduced tendency to oligomerize, and are not ambiguous. Accordingly, Applicants respectfully submit that the rejections of Claims 115-118, 121, 125, 128, and 148-162 under 35 U.S.C. §112, second paragraph, is overcome.

### **CONCLUSION**

Applicants request the entry of the above amendments, which are believed to place the claims in condition for allowance or in better form for consideration on appeal. It is emphasized that the claim amendments were made without prejudice, and without acquiescence to the present rejections or the Examiner's reasoning underlying the present rejections. Applicants specifically reserve the right to pursue any subject matter not within the scope of the present claims in one or more continuing applications.

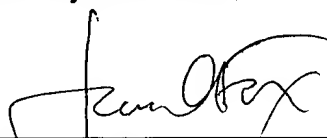
Applicants respectfully submit that all claim rejections and objections are overcome by the above arguments and amendments, and request reconsideration and allowance of all pending claims. An early indication of their allowance is earnestly requested. The Examiner is invited to contact the undersigned attorney at the telephone number indicated below should he find that there are any further issues outstanding.

Although no fees are believed to be due at this time, please charge any fees, including any fees for extension of time, or credit overpayment to Deposit Account No. **08-1641** referencing Attorney's Docket No. **39754-0891 CPC1CP1**.

Respectfully submitted,

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By:

  
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